peptide selection

↓

peptide optimization

formation of Fc-peptide DNA construct

l

insertion of construct into expression vector

L

transfection of host cell with vector



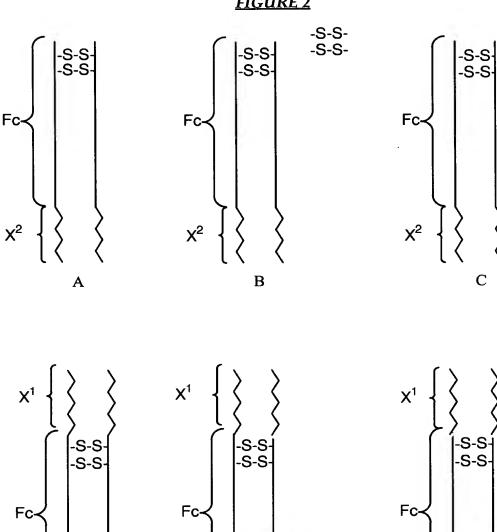
expression of vector in host cell



Fc multimer formation in host cell



isolation of Fc multimer from host cell



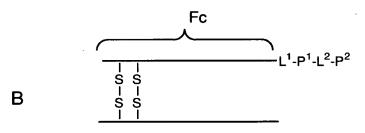
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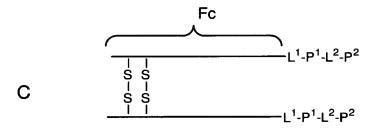
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F









							_		un		_							. ~ ~ .		
	1	ATGG			CACAC															60
	•	TACCI																		
a		M D	K	T	н т	С	P	P	С	P	A	P	E	L	L	G	G	P	S	-
	<b>61</b>	GTCTT																		120
	0.1	CAGAZ																		120
a		V F	L	F	P P	K	P	ĸ	D	T	L	М	I	s	R	T	P	E	v	-
		ACATO	CGT:	GGTG	GTGG	ACGT	GAG	CCAC	CGA/	AGA(	ccc:	rgac	GTC	CAAC	STTC	CAAC	CTG	GTAC	CGTG	
	121	TGTAC																		180
a		т с	v	v	V D	v	s	Н	E	D	P	E	v	K	F	N	W	Y	v	-
		GACGO																		
	181	CTGCC																		240
a		D G	v	E	v н	N	A	ĸ	т	ĸ	P	R	E	E	Q	Y	N	s	T	-
		TACCO																		
	241	ATGGO																		300
a		Y R	v	v	s v	L	T	v	L	Н	Q	D	W	L	N	G	K	E	Y	-
		AAGT																		
	301	TTCAC																		360
a		к с	K	v	s n	K	A	L	P	A	P	I	E	ĸ	T	I	s	ĸ	A	-
		AAAGG																		400
	361	TTTCC																		420
a		K G	Q	P	R E	P	Q	v	Y	т	L	P	P	s	R	D	E	L	T	-
		AAGA																		
	421	TTCTT			TCGG															480
a		K N	Q	v	s L	T	С	L	v	ĸ	G	F	Y	P	s	D	I	Α	v	-
		GAGTO																		
	481	CTCAC																		540
a		E W	E	s	N G	Q	P	E	N	N	Y	ĸ	т	T	P	P	v	L	D	-
		TCCG																		
	541	AGGCT																		600
a		s D	G	s	F F	L	Y	s	ĸ	L	т	v	D	ĸ	s	R	W	Q	Q	-
		GGGAA																		
	601	CCCTI																		660
a		G N	v	F	s c	s	v	М	н	E	A	L	H	N	Н	Y	Т	Q	ĸ	-
		AGCCT																		
	661	TCGGA							584											
a		S L	s	L	S P	G	ĸ													

		XDA1	
		TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC	
c	1	AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCTGTTTTGAGTGTGTACAG  M D K T H T C P	
•	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	
с		GTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGCAGTCAGAAGGAGGAGGAGGGGGTTTTG P C P A P E L L G G P S V F L F P P K P	-
C	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA  GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCACCACC  K D T L M I S R T P E V T C V V V D V S	180 -
	181	$\tt CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC$	
С	0.4.1	CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA	
С	241	GGTTCTGTTTCGGCGCCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT  K T K P R E E Q Y N S T Y R V V S V L T	
<b>~</b>	301	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
Č	361	CCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC	
С	301	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	421	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	480 -
c	481	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCTCTCT GCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGAAGAAGA	
С	601	E N N Y K T T P P V L D S D G S F F L Y  ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG	
С		TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC S K L T V D K S R W Q Q G N V F S C S V	-
С	661	TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA + CTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT M H E A L H N H Y T Q K S L S L S P G K	
	721	AAGGTGGAGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGGC	780
С		G G G G I E G P T L R Q W L A A R A *  BamHI	-
	781	AATCTCGAGGATCC	
		TTAGAGCTCCTAGG	

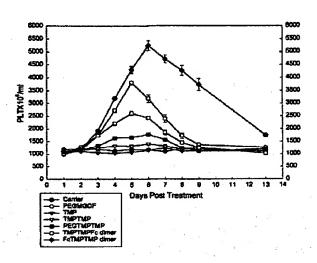
	XŁ	paI	
	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC	60
С		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	120
с		GTGGAACAGGTCGAGGCCTTGAGGACCCCCCTGGCAGTCAGAAGGAGAAGGGGGGTTTTG P C P A P E L L G G P S V F L F P P K P	-
	121	GGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGCACT	
С		K D T L M I S R T P E V T C V V D V S  GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATG	-
_	181		
С		CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA	
c	241	GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAGTCGCAGGAGT  K T K P R E E Q Y N S T Y R V V S V L T	
_		CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG	250
С	301	GGCAGGACGTGGTCCTGACCGACTTACCGTTCCTCATGTTCACGTTCCAGAGGTTGTTTC V L H Q D W L N G K E Y K C K V S N K A	
	361	CCCTCCCAGCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC	420
c	301	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	421	AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT+ TCCACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA	480
С		V Y T L P P S R D E L T K N Q V S L T C	•
С	481	GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC  CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG  L V K G F Y P S D I A V E W E S N G Q P	
	541	CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT	600
С	341	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	601		660
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	661		720
c		ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT M H E A L H N H Y T Q K S L S L S P G K	-
С	721	AAGGTGGAGGTGGTATCGAAGGTCCGACTCTGCGTCAGTGGCTGCTCGTGCTG  TTCCACCTCCACCACCATAGCTTCCAGGCTGAGACGCAGTCACCGACCG	
	721	GTGGTGGAGGTGGCGGGGGGGTATTGAGGGCCCAACCCTTCGCCAATGGCTTGCAGCAC	840
с	,01	CACCACCTCCACCGCCGCCTCCATAACTCCCGGGTTGGGAAGCGGTTACCGAACGTCGTG G G G G G I E G P T L R Q W L A A R	
	011	BamHI   GCGCATAATCTCGAGGATCCG	

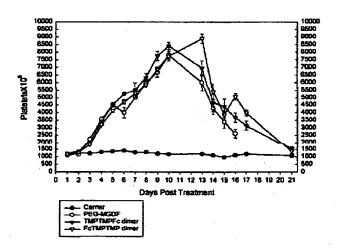
841 ----+---+- 861 CGCGTATTAGAGCTCCTAGGC

	2	(baI	
	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGATCGAAGGTCCGACTCTGC	60
С		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	61	GTCAGTGGCTGGCTGGCGGTGGCGGGGGGGGGGGCATTGAGGGCCCAA CAGTCACCGACCGACGACGACGACGACGCCACCACCGCTAACTCCCGGGTT	120
c		Q W L A A R A G G G G G G G I E G P T	•
c	121	CCCTTCGCCAATGCTTGCAGCACGCGCAGGGGGAGGCGGTGGGGACAAAACTCACACAT  GGGAAGCGGTTACCGAACGTCGTGCGCGCCCCCTCCGCCACCCCTGTTTTGAGTGTGTA  L R O W L A A R A G G G G G D K T H T C	
	181	GTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAA	240
c	101	CAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAAGGGGGGTT PPCPAPELLGGPSVFLFPPK	
	241	AACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACG TTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCACCACCTGC	300
С		P K D T L M I S R T P E V T C V V V D V  TGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATA	-
С	301	ACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCACGTAT S H E D P E V K F N W Y V D G V E V H N	
С	361	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
С	421	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	481	AAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAAC TTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTG	
С		A L P A P I E K T I S K A K G Q P R E P  CACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGA	-
С	541	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	601	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	660 -
С	661	AGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCC  TCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGCCGAGGAAGAAGG PENNNYKTPPPVLDSDGGAGGACGACCTGAGGCTGCCGAGGAAGAAGG	720
	721	TCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCT  AGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGA	780
С	781	Y S K L T V D K S R W Q Q G N V F S C S  CCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG	
c		GGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCC V M H E A L H N H Y T Q K S L S L S P G BamHI	-
	841	GTAAATAATGGATCC	

С

	2	KbaI	
с	1	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGATCGAAGGTCCGACTCTGC  AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACTAGCTTCCAGGCTGAGACG  M I E G P T L R	
С	61	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	121	CTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCCTCTTCCCCCCAAAACCCA  GAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGGAGAAGGGGGGTTTTGGGT C P A P E L L G G P S V F L F P P K P K	
с	181	AGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCC	
c	241	ACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGCACGCGCGTGGAGGTGCATAATGCCA  TGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGT  E D P E V K F N W Y V D G V E V H N A K	
c	301	AGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCG  TCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACCACCAGTCGCAGGAGTGGC TKPREEQYNSTYRVVSSVLTV	
c	361	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	421	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	481	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
С	541	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	601	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	661	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	721	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	781	BamHI   AATGGATCC 789 TTACCTAGG	





	2	XbaI	
	,	TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC	60
С	1	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	61	CACCTTGTCCAGCTCCGGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAAC	120
С		P C P A P E L L G G P S V F L F P P K P	-
	121	CCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGA	180
c		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	181	GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATG	240
с		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	241	CCAAGACAAAGCCGCGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCA	300
c		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	301	CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAG	360
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
		CTCCCAGCCCCATCGAGAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC	420
С		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	421	AGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT	480
С		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
	481	GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGACAATGGGCAGC	540
c		CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCCTCTCGTTACCCGTCG L V K G F Y P S D I A V E W E S N G Q P CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT	-
	541	GCCTCTTGTTGATGTTCTGGTGCGGAGGCACGACCTGAGGCTGCCGAGGAAGAAGAAGAAGAGA	
С		E N N Y K T T P P V L D S D G S F F L Y  ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG	-
	601	TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC	
C		S K L T V D K S R W Q Q G N V F S C S V  TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA	•
	661	ACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGCAGAGGCCCAT	720
С		M H E A L H N H Y T Q K S L S L S P G K  AAGGTGGAGGTGGTGGAGGTACTTACTCTTGCCACTTCGGCCCGCTGACTTGGGTTT	•
	721	TTCCACCTCCACCACCACCATGAATGAGAACGGTGAAGCCGGGCGACTGAACCCAAA	
С		G G G G G G T Y S C H F G P L T W V C  BamHI	
		ĺ	
	781	GCAAACCGCAGGGTGGTTAATCTCGTGGATCC	

GCAAACCGCAGGGTGGTTAATCTCGTGGATCC
781
CGTTTGGCGTCCCACCAATTAGAGCACCTAGG
K P Q G G \*

C

	XbaI   TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGGAGGTACTTACT	
С	1+ 6 AGATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCCTCCATGAATGA	
	ACTTCGGCCCGCTGACTTGGGTATGTAAGCCACAAGGGGGTGGGGGGGG	
1:	AAACTCACACATGTCCACCTTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTTTTCC  TTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCCCCTGGCAGTCAAAAGG	
С	T H T C P P C P A P E L L G G P S V F L TCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCG	
c	1+ + + + + + + + + + + + + + + + +	
2 ·	TGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG  ACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGC  V V D V S H E D P E V K F N W Y V D G V	
	TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTG  ACCTCCACGTATTACGGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCAC EVHNAKTKPREEQVXNSTYRV	360
	TGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA  ACCAGTCGCAGGAGTGGCAGGACGTGGTCCTGACCGTTCCTCATGTTCACGT  V S V L T V L H Q D W L N G K E Y K C K	420
4: C	AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGCC 1	
4: C	AGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACC  TCGGGGCTCTTGGTGTCCACATGTGGGACGGGGTAGGGCCCTACTCGACTGGTTCTTGG PREPQVYTLPPSRDELTKNQ	
5·	AGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGG  TCCAGTCGGACTGGACGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCC V S L T C L V K G F Y P S D I A V E W E	600 -
6: C	AGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG  TCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGGCACGACCTGAGGCTGC S N G Q P E N N Y K T T P P V L D S D G	
6: C	GCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACG  CGAGGAAGAAGAAGAGATGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGC S F F L Y S K L T V D K S R W Q Q G N V	720 -
7: c	TCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT  AGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGA  F S C S V M H E A L H N H Y T Q K S L S	
	BamHI	
7	CCCTGTCTCCGGGTAAATAATGGATCC  1	

	XI	DAI     TCTAGATTTGAGTTTTAACTTTTAGAAGGAGGAATAAAATATGGGAGGTACTTACT	60
b	1	AGATCTAAACTCAAAATTGAAAATCTTCCTCCTTATTTTATACCCTCCATGAATGA	-
	- 1	$\tt CCACTTCGGCCCACTGACTTGGGTTTGCAAACCGCAGGGTGGCGGCGGCGGCGGCGGTGG$	100
ь	61	GGTGAAGCCGGGTGACCGAACCCAAACGTTTGGCGTCCCACCGCCGCCGCCGCCACC H F G P L T W V C K P Q G G G G G G	-
b	121	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	180 -
b	181	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	240 -
	241	ACCGTCAGTTTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC	300
b	241	TGGCAGTCAAAAGGAGAAGGGGGTTTTGGGTTCCTGTGGGAGTACTAGAGGGCCTGGGG PSVFLFPPKPKDTLMISRTP	-
b	301	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	360 -
b	361	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	420 -
b	421	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	480 -
b	481	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	540 -
b	541	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	600 -
b	601	GCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACAT +	660
2	661	CGCCGTGGAGTGGGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGT	720
b		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-
b	721	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	780 -
b	781	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	840 -
		BamHI	
b	841	GCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGATCC+ 881 CGTCTTCTCGGAGAGGGACAGAGGCCCATTTATTACCTAGG Q K S L S L S P G K *	

#### A-527

С

## FICUIDE 16

<u>FIG</u>			
c		(bai     TCTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGACAAAACTCACACATGTC  ++++++	
c	61	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
c	121	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	181	GCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATG  CGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC  H E D P E V K F N W Y V D G V E V H N A	
с	241	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	301	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	361	CCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAC GGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGGGGCTCTTGGTG L P A P I E K T I S K A K G Q P R E P Q	
с	421	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	481	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	541	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	601	ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG  TGTCGTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCCCTTGCAGAAGAGTACGAGGC S K L T V D K S R W Q Q G N V F S C S V	
c	661	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
с	721	AAGGTGGAGGTGGCGGAGGTACTTACTCTTGCCACTTCGGCCCACTGACTTGGGTTT  TTCCACCTCCACCACCGCCTCCATGAATGAGAACGGTGAAGCCGGGTGACCCAAA G G G G G G T Y S C H F G P L T W V C	
С	781	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
		BamHI   TGACCTGGGTATGTAAGCCACAAGGGGGTTAATCTCGAGGATCC	

#### FIGURE 17A

[AatII :	sti	.cky	en	d]	
(position	on	#435	8	in	pAMG21)

- 5' GCGTAACGTATGCATGGTCTCC-
- 3 ' TGCACGCATTGCATACGTACCAGAGG-
- CCATGCGAGAGTAGGGAACTGCCAGGCATCAAATAAAACGAAAGGCTCAGTCGAAAGACT GGTACGCTCTCATCCCTTGACGGTCCGTAGTTTATTTTGCTTTCCGAGTCAGCTTTCTGA -
- GGGCCTTTCGTTTTATCTGTTGTTTGTCGGTGAACGCTCTCCTGAGTAGGACAAATCCGC CCCGGAAAGCAAAATAGACAACAAACAGCCACTTGCGAGAGGACTCATCCTGTTTAGGCG -
- CGGGAGCGGATTTGAACGTTGCGAAGCAACGCCCGGAGGGTGGCGGGCAGGACGCCCGC GCCCTCGCCTAAACTTGCAACGCTTCGTTGCCGGGCCTCCCACCGCCCGTCCTGCGGGCG
- CATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCTGACGGATGGCCTTTTTTGCGT GTATTTGACGGTCCGTAGTTTAATTCGTCTTCCGGTAGGACTGCCTACCGGAAAAACGCA -

#### AatII

- TTCTACAAACTCTTTTGTTTATTTTTCTAAATACATTCAAATATGGACGTCGTACTTAAC AAGATGTTTGAGAAAACAAATAAAAAGATTTATGTAAGTTTATACCTGCAGCATGAATTG -
- $\mathtt{TTTTAAAGTATGGGCAATCAATTGCTCCTGTTAAAATTGCTTTAGAAATACTTTGGCAGC-AAAATTTCATACCGGTTAGTTAACGAGGACAATTTTAACGAAATCTTTATGAAACCGTCG-$
- GGTTTGTTGTATTGAGTTTCATTTGCGCATTGGTTAAATGGAAAGTGACCGTGCGCTTAC-CCAAACAACATAACTCAAAGTAAACGCGTAACCAATTTACCTTTCACTGGCACGCGAATG-
- $\hbox{-} TACAGCCTAATATTTTTGAAATATCCCAAGAGCTTTTTCCTTCGCATGCCCACGCTAAAC-ATGTCGGATTATAAAAACTTTATAGGGTTCTCGAAAAAGGAAGCGTACGGGTGCGATTTG-$
- GATAATTATCAACTAGAGAAGGAACAATTAATGGTATGTTCATACACGCATGTAAAAATA-CTATTAATAGTTGATCTCTTCCTTGTTAATTACCATACAAGTATGTGCGTACATTTTAT-
- AACTATCTATATAGTTGTCTTTCTCTGAATGTGCAAAACTAAGCATTCCGAAGCCATTAT-TTGATAGATATATCAACAGAAAGAGACTTACACGTTTTGATTCGTAAGGCTTCGGTAATA-
- TAGCAGTATGAATAGGGAAACTAAACCCAGTGATAAGACCTGATGATTTCGCTTCTTTAA-ATCGTCATACTTATCCCTTTGATTTGGGTCACTATTCTGGACTACTAAAGCGAAGAAATT-
- TTACATTTGGAGATTTTTTATTTACAGCATTGTTTTCAAATATATTCCAATTAATCGGTG AATGTAAACCTCTAAAAAATAAATGTCGTAACAAAAGTTTATATAAGGTTAATTAGCCAC -
- AATGATTGGAGTTAGAATAATCTACTATAGGATCATATTTTATTAAATTAGCGTCATCAT TTACTAACCTCAATCTTATTAGATGATATCCTAGTATAAAATAATTTAATCGCAGTAGTA -
- AATATTGCCTCCATTTTTTAGGGTAATTATCCAGAATTGAAATATCAGATTTAACCATAG-TTATAACGGAGGTAAAAAATCCCATTAATAGGTCTTAACTTTATAGTCTAAATTGGTATC-TTATAGTCTAAATTGGTATTGAAATTGGTATC-TTATAGTCTAAATTGGTATTGAAATTGGTATGAAATTGGTATGAAATTGGTAAATTGGTATTGAAATTGGTATGAAATTGAAAATTGAAATTGAAATTGAAATTGAAATTGAAATTGAAATTGAAAATTGAAAATTGAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAATTGAAAATTGAAATTGAAATTGAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAATTGAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAAATTGAAATTAAATTGAAAATTGAAATTGAAATTGAAATTGAAATTGAAAATTGAAAATTGAAAATTGAAAATT
- AATGAGGATAAATGATCGCGAGTAAATAATATTCACAATGTACCATTTTAGTCATATCAG-- TTACTCCTATTTACTAGCGCTCATTTATTATAAGTGTTACATGGTAAAATCAGTATAGTC -

- -GCAAGTTTTGCGTGTTATATATCATTAAAACGGTAATAGATTGACATTTGATTCTAATAA
- -CGTTCAAAACGCACAATATATAGTAATTTTGCCATTATCTAACTGTAAACTAAGATTATT-

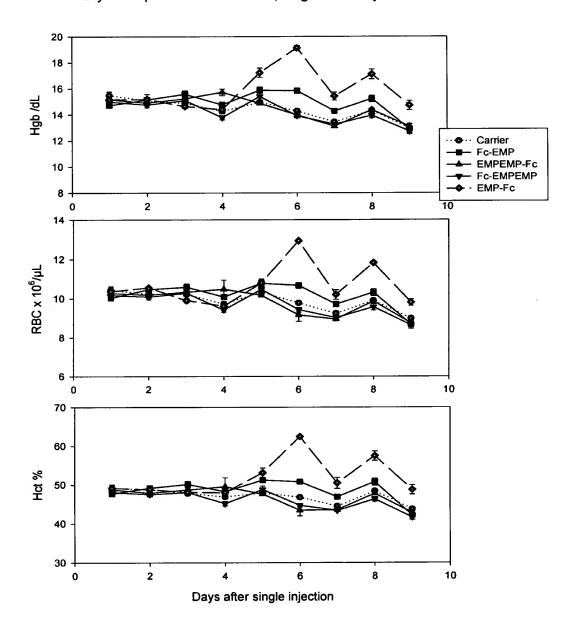
#### FIGURE 17B

- ATTGGATTTTTGTCACACTATTATATCGCTTGAAATACAATTGTTTAACATAAGTACCTG - TAACCTAAAAACAGTGTGATAATATAGCGAACTTTATGTTAACAAATTGTATTCATGGAC -
- TAGGATCGTACAGGTTTACGCAAGAAAATGGTTTGTTATAGTCGATTAATCGATTTGATT - $\hbox{-ATCCTAGCATGTCCAAATGCGTTCTTTTACCAAACAATATCAGCTAATTAGCTAAACTAA} - \hbox{-}$
- $\hbox{-} \mathtt{CTAGATTTGTTTTAACTAATTAAAGGAGGAATAACATATGGTTAACGCGTTGGAATTCGA-}$  $\hbox{-} {\tt GATCTAAACAAAATTGATTAATTTCCTCCTTATTGTATACCAATTGCGCAACCTTAAGCT-}$

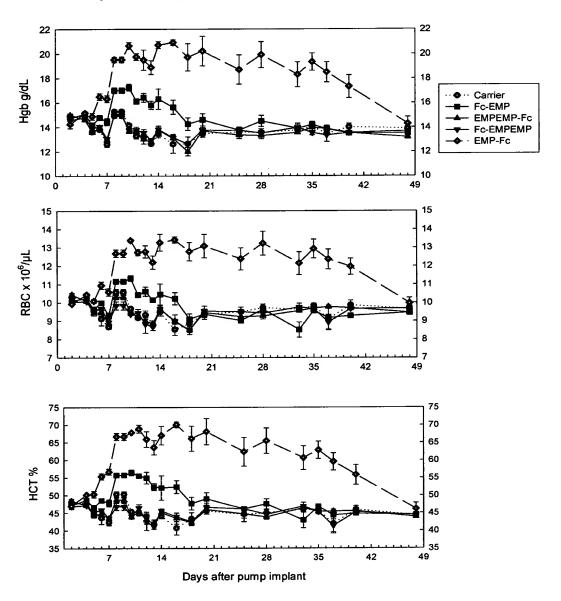
#### <u>Sac</u>II

- -GCTCACTAGTGTCGACCTGCAGGGTACCATGGAAGCTTACTCGAGGATCCGCGGAAAGAA- $\hbox{-} \textbf{CGAGTGATCACAGCTGGACGTCCCATGGTACCTTCGAATGAGCTCCTAGGCGCCTTTCTT-}$
- GAAGAAGAAGAAGCCCGAAAGGAAGCTGAGTTGGCTGCCACCGCTGAGCAATA - $\hbox{-} \mathtt{CTTCTTCTTCTTCGGGCTTTCCTTCGACTCAACCGACGGTGGCGACTCGTTAT-}$
- $\hbox{-} ACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGGGGGTTTTTTTGCTGAAAGGAGG \hbox{-} {\tt TGATCGTATTGGGGAACCCCGGAGATTTGCCCAGAACTCCCCAAAAAACGACTTTCCTCC-}$
- -AACCGCTCTTCACGC 3' [SacII sticky end]
  -TTGGCGAGAAGTGCGAGAAGTG 5' (position #5904 in pAMG21) -AACCGCTCTTCACGCTCTTCACGC 3'

Erythroid parameters EMP-Fc, single bolus injection.



Normal female BDF1 mice treated with 100ug/kg EMP-Fc in 7-day micro osmotic pumps



## FIGURE 19A

	Ndel	 CAT	ATGG	ACAA	AAC	TCA	CAC.	ATG	TCC.	ACC	TTG	TCC.	AGC'	TCC	GGA.	ACT	CCTO	GGG	GG2	ACCG	<b>C</b> 0
	1	GTA'	racc'																	rggc	60
a		1	M D	ĸ	т	Н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
	61		GTCT'  CAGA	+ -			+				+			-+-			+			+	120
a		S ·	V F	L	F	P	P	K	P	K	D	T	L	M	I	s	R	Т	P	E	-
	121		ACAT  TGTA	+ -			+				+			-+-			+			+	180
a		V	т с	V	v	V	D	V	s	Н	E	D	P	E	V	K	F	N	W	Y	-
	181		GACG  CTGC	+-			+				+			-+-			+			+	240
a		V :	D G	V	E	V	Н	N	A	K	т	ĸ	P	R	E	E	Q	Y	N	S	-
	241		TACC  ATGG	+-			+				+			-+-			+			+	300
a		T	Y R	V	V	s	V	L	Т	V	L	Н	Q	D	W	L	N	G	K	E	-
	301		AAGT  TTCA	+-			+				+			- <b>+ -</b>			+			<del>+</del> GTTT	360
a		_	K C				N				P		P	I	Ε	K	Т	I	S	K	-
	361		AAAG  TTTC	+ -		- <b></b>	+				+			-+-			+			+	420
a		A	K G	Q	P	R	E	P	Q	V	Y	Т	L	P	P	S	R	D	E	L	-
	421		AAGA  TTCT	+ -		<b>-</b>	+				+			-+-			+			+	480
a		Т	K N	Q	v	s	L	T	С	L	v	K	G	F	Y	P	S	D	I	A	-
	481		GAGT  CTCA	+-	- <b></b>		+	- <b></b>			+			-+-			+			GCTG + CGAC	540
a		v	E W	E	S	N	G	Q	P	E	N	N	Y	K	Т	т	P	P	V	L	-
	541		TCCG  AGGC	+ -			+				+			-+-			+			+	600
a		D	s D	G	S	F	F	L	Y	S	K	L	T	V	D	K	S	R	W	Q	-

# FIGURE 19B

	601	CA	GGG	GAA(	CGT(	CTT(	CTC	ATG( +	CTC	CGT	GAT	GCA' +	TGA	GGC	TCT -+-	GCA	CAA	CCA	CTA	CAC	GCAG	660
	001	GT	GTCCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTC																			
a		Q	G	N	v	F	s	С	S	v	М	Н	E	A	L	Н	N	Н	Y	Т	Q	-
	661				-+-			+				+	<b>-</b>		-+-			+			CTAC + GATG	720
a		K	s	L	s	L	s	P	G	к	G	G	G	G	G	D	F	L	P	Н	Y	-
											Ва	mHI 										
	721	- <b>-</b>	AAA(  TTT(		- + -			+				+		<b>-</b> -	757							
				_	_	_	_	••	_	_	_											

#### FIGURE 20A

		Nde 																			
	1		TGGA  ACCT	-+-			+				+			-+-		·	-+-	. <b></b> .		+	60
a		M	ı D	F	L	P	Н	Y	ĸ	N	т	s	L	G	н	R	P	G	G	G	-
	61		GGGA	-+-			+				+			- + -			+ -			+	120
a		GCAC	CCCT	'GTT	TTG. Т	AGT H	GTG T	TAC.	AGG <sup>.</sup> P	rGG,	AAC(	eGG. P	rcg.	P P	ACT.	rga( L	L	G	G	P	_
_	121	TCAG	TTTTT 	-+-			+				+			- + -			+ -			+	180
a		s v	7 F	L	F	P	P	K	P	K	D	т	L	М	I	s	R	T	P	E	-
	181		CATO	-+-			+				+			- + -			+ -			+	240
a		r v	c C	V	V	v	D	v	s	Н	E	D	P	E	V	K	F	N	W	Y	-
	241		ACGC TGCC	-+-			+				+			- + -			+ -			+	300
a		V I	G	V	E	v	Н	N	A	K	Т	K	P	R	E	E	Q	Y	N	S	-
	301		TGGC	-+-			+				+			-+-			+ -			+	360
a		T Y	R	V	V	s	v	L	т	v	L	H	Q	D	W	L	N	G	ĸ	Ε .	-
	361		AGTO TCAC	-+-			+				+			- + -			+ -			+	420
a		Y F	C	K	V	s	N	K	A	L	P	A	P	I	E	K	T	I	S	K	-
	421		AAGG	-+-			+				+			-+-			+ -	:		+	480
a		A F	G	Q	P	R	E	P	Q	v	Y	T	L	P	P	s	R	D	E	L	-
	481		AGAA	-+-			+				+			-+-			+ -			+	540
a		т н	N	Q	v	s	L	T	С	L.	v	K	G	F	Y	P	s	D	I	A	-
	541		SAGTO CTCAC	-+-			+				+			- + -			+			+	600
a		V E	e w	E	s	N	G	Q	P	E	N	N	Y	ĸ	т	т	P	P	v	L	-

## FIGURE 20B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
a		D	S	D	G	s	F	F	L	Y	s	K	L	T	v	D	K	s	R	W	Q	-
	661				-+-			+				+			-+-	- <b></b>		+			GCAG + CGTC	720
a		Q	G	N	V	F	S	С	S	v	М	Н	Е	A	L	Н	N	Н	Y	Т	Q	-
	721				-+-	GGA		+ AGG	CCC	 ATT	АТА  ТАТ	mHI   ATG + TAC			-+-	76	1					

#### FIGURE 21A

	No	leI I																			
	1	CAT	ATGGA				CAC									ACTO	CCTC	GGG	GGA	ACCG	60
	1		PACCT	•												rga(	GGAC	ccc	CCI		•
a		ı	M D	K	T	Н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
			<b>ЭТСТТ</b>	ССТ	СТТ	ccc														rgag	120
	61		CAGAA	GGA	GAA	GGG												CTGC		ACTC	120
a		s ·	V F	L	F	P	P	ĸ	P	ĸ	D	т	L	M	I	s	R	T	P	E	-
		GTC	ACATG	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA	AGA	ccc′	rga(	GGT	CAAC	3TTC	CAAC	TGC	STAC	
	121		 TGTAC																		180
a		v :	r c	v	v	v	D	v	s	н	E	D	P	E	v	K	F	N	W	Y	-
			GACGG																		
	181		CTGCC																		240
a		V I	D G	v	Е	v	н	N	A	K	т	K	P	R	E	E	Q	Y	N	S	-
		ACG'	TACCG	TGT	GGT	CAG	CGT	ССТ	CAC	CGT	ССТ	GCA	CCA	GGA(	CTG	GCT	GAA:	rggo	CAAC	GAG	
	241		 ATGGC	-+-			+				+			-+-			+ -		·	+	300
a			y R	V	v	S	v	L	т	v	L	Н	0	D	W	L	N	G	ĸ	E	-
-		TAC	AAGTG	CAA	GGT	СТС	CAA	CAA	AGC	CCT	CCC.	AGC	CCC	CAT	CGA	GAA	AAC	CATO	CTCC	CAAA	
	301	 ATG'	TTCAC	•			+ GTT				-						+ · rtg(	GTA(	GAG	+ 3TTT	360
a			K C	ĸ	v	s	N	ĸ	A	L	P	A	P	I	E	ĸ	т	I	s	ĸ	_
_			AAAGG		•	-	_			– GGT	- GTA	CAC	- ССТ	GCC	ccc	ATC	CCG	GGA	rgao	GCTG	
	361		TTTCC	-+-			+				+			- + -			+			+	420
a					P	R	E	P		v			L		P	s	R	D	E	L	_
a			AAGAA	~	_		_	_	~			-	_	_	_	_		_	_	_	
	421		TTCTI	-+-			+				+			-+-			+	:		+	480
_			K N							-											_
a			K N GAGTO																		
	481		CTCAC	-+-			+				+			-+-			+			+	540
																					_
a			E W																		-
	541		TCCGA	-+-			+				+			-+-			+			+	600
			AGGCT																		
a		D :	S D	G	S	F	F	L	Y	S	K	L	т	V	D	K	S	R	W	Q	-

## FIGURE 21B

	C 0 1	CAG	GGG(	GAA(	CGT	CTT	CTC	ATG	CTC	CGT	GAT	GCA	TGA(	GGC'	ГСТ <sup>.</sup> - + -	GCA	CAA	CCA(	CTA	CAC	GCAG	660
	601	GT	CCC	CTT	GCA	GAA(						-									CGTC	
a		Q	G	N	V	F	s	С	s	V	M	Н	E	A	L	Н	N	Н	Y	Т	Q	-
•	661				-+-			+				+			-+-			+			GGGT + CCCA	720
a		K	s	L	s	L	S	P	G	K	G	G	G	G	G	F	E	W	T	P	G	-
											Ва	mHI.										
	721				GCC -+- CGG			+				+			-+-		763					
3		v	TAT	Λ	Ð	v	Δ	т.	p	Τ.	*											

## FIGURE 22A

		Nd	eI																		
				TTCGA														GGG'	rggz		60
	1			AAGCI														CCC	ACCT		00
a			M I	E	W	Т	P	G	Y	W	Q	P	Y	A	L	P	L	G	G	G	-
	61			GACAA +- CTGTT	. <b></b> -		+				+			- + -			+			+	120
a				о к	т	н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
		тса	Gጥጥ	rtcci	СТТ	ccc	ccc	AAA	ACC	CAA	GGA	CAC	ССТ	САТ	GAT	CTC	CCG	GAC	ccci	rgag	
	121			AAGGA			+				+		<b>-</b> - <b>-</b>	-+-			+			+	180
a				F L	F	P	P	K	P	K	D	т	L	M	I	s	R	т	P	Е	-
		GTC	'ACA'	rgcgi	rggī	GGT	GGA	CGT	GAG	CCA	CGA	AGA	CCC	TGA	GGT	CAA	GTT(	CAA	CTG	GTAC	
	181			+ - ACGC			+				+			-+-			+			+	240
a				c v		v		v		Н	E		P		v	K	F	N	W	Y	-
		GTG	GAC	GGCG1	rgga	GGT	GCA	таа	TGC	CAA	GAC	AAA	GCC	GCG	GGA	GGA	GCA	GTA(	CAA	CAGC	
	241			+ - CCGC <i>I</i>			+				+			-+-			+			+	300
a		v	D (	g V	Е	v	н	N	Α	ĸ	т	K	P	R	E	E	Q	Y	N	s	-
		ACG	TAC	CGTGT	rggī	CAG	CGT	ССТ	CAC	CGT	ССТ	GCA	CCA	GGA	.CTG	GCT	GAA'	TGG	CAA	GGAG	
	301			GCAC			+				+			- + -			+			+	360
a		т		R V	v	s	V	L	т	v	L	Н	Q	D	W	L	N	G	K	E	-
		TAC	'AAG'	TGCA?	AGGI	CTC	CAA	.CAA	AGC	ССТ	ccc	AGC	ccc	CAT	CGA	GAA	AAC	CAT	CTC	CAAA	
	361			ACGTT			+				+			-+-			+			+	420
a		Y	K (	с к	v	s	N	ĸ	Α	L	P	Α	P	I	E	K	т	I	s	K	_
		GCC	'AAA	GGGC <i>I</i>	AGCC	cce	AGA	ACC	ACA	GGT	GTA	CAC	CCT	GCC	ccc	ATC	CCG	GGA'	rga(	GCTG	
	421	CGG	 TTTC	+ CCCG1																+ CGAC	480
a		A	K (	G Q	P	R	E	P	Q	v	Y	Т	L	P	P	s	R	D	E	L	-
		ACC	AAG	AACC	AGGI	CAG	CCT	GAC	CTG	CCT	GGT	CAA	AGG	СТТ	СТА	TCC	CAG	CGA	CAT	CGCC	
	481			+ TTGGT																	540
a		т	K 1	N Q	v	s	L	т	С	L	V	ĸ	G	F	Y	P	s	D	I	A	-
				TGGG																	
	541	CAC	CTC	ACCCI	rctc	GTT	+ 'ACC	CGT	CGG	CCT	+ 'CTT	GTT	GAT	- + - GTT	CTG	GTG	+ CGG	agg	GCA	CGAC	600
a		v	E '	W E	s	N	G	Q	P	E	N	N	Y	K	т	т	P	P	v	L	-

#### FIGURE 22B

	601				-+-			+				+			-+-			+			GCAG + CGTC	660
a		D	s	D	G	s	F	F	L	Y	s	K	L	T	v	D	K	s	R	W	Q	-
	661				-+-			+				+			-+-			+			GCAG + CGTC	720
a		Q	G	N	V	F	S	С	s	v	M	Н	E	A	L	Н	N	Н	Y	T	Q	-
											Ва	mHI										
	721				- + -			+				ATG + TAC			75 <b>7</b>							
_		v	œ	τ.	Q	τ.	Q	Ð	G	ĸ	*											

## FIGURE 23A

	Nd	eI																				
	1	CAT	'ΑΤΟ	GAG	CAA	AAC'	rca(	CACA	ATG	rcc <i>i</i>	ACC	GTG(	CCC	AGC	ACC	rga.	ACTO	CTC	GGC	GGA	CCG	60
	1	GTA	TAC	CTC	3TTT	rtgi	AGT	3TG:	raca	AGGT	rgg(	CAC	GGT	rcgi	rggz	ACTT	rGAG	GAC	CCC	CCT	GGC	
a			M	D	K	Т	Н	Т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
	<b>C1</b>		GT?	rtt(	ССТС	CTT(	ccc	CCC	AAA	ACC	CAA	GGA(	CAC	CCT	CAT(	GAT	CTCC	CCGC	ACC	CCI	GAG	120
	61	AGI	CA	\AA(	GGA	GAA	GGG	GGG'	rtt	rgg(	GTT(	CCT	GTG	GGA(	TAC	CTA	GAGO	GCC	CTGC	GGZ	CTC	
a		S	V	F	L	F	P	P	ĸ	P	K	D	т	L	M	I	s	R	T	P	E	-
	121		AC	ATG(	CGT	GGT	GGT(	GGA(	CGT	GAG	CCA	CGA	AGA	CCC	rga(	GGT(	CAAC	3TT(	CAAC	CTGC	TAC	180
	121	CAG	TG'	rac	GCA	CCA	CCA	CCT	GCA	CTC	GGT	GCT'	тсто	GGG	ACT	CCA	GTT(	CAA	GTT(	GACC	CATG	
a		V	т	С	V	v	v	D	V	S	Н	E	D	P	E	V	K	F	N	W	Y	-
	181	GTC	GA	CGG	CGT	GGA	GGT	GCA	TAA'	TGC	CAA	GAC.	AAA(	GCC	GCG	GGA	GGA(	GCA(	GTA(	CAA	CAGC	240
	101	CAC	CT	GCC	GCA	CCT	CCA	CGT.	ATT.	ACG	GTT	CTG	TTT	CGG	CGC	CCT	CCT	CGT	CAT	GTT(	STCG	
a		v	D	G	V	E	v	Н	N	A	K	Т	K	P	R	E	E	Q	Y	N	S	-
	241	ACC	TA:	CCG	TGT	GGT	CAG	CGT	CCT	CAC	CGT	ССТ +	GCA	CCA	GGA	CTG	GCT(	GAA'	rgg(	CAA	GAG	300
	241	TGO	CAT	GGC.	ACA	CCA	GTC	GCA	GGA	GTG	GCA	GGA	CGT	GGT	CCT	GAC	CGA	CTT	ACC	GTT(	CCTC	
a		Т	Y	R	V	V	s	V	L	T	V	L	Н	Q	D	W	L	N	G	K	E	-
	301	TAC	CAA	GTG	CAA	GGT	CTC	CAA	CAA	AGC	CCT	CCC +	AGC	CCC	CAT	CGA	GAA.	AAC(	CAT(	CTC	CAAA +	360
	301	ATO	3TT	CAC	GTT	CCA	GAG	GTT	GTT	TCG	GGA	GGG	TCG	GGG	GTA	GCT	CTT'	TTG	GTA	GAG	GTTT	
a		Y	K	С	K	V	S	N	K	A	L	P	A	P	I	E	K	Т	I	S	K	-
	361	GC	CAA	AGG	GCA	GCC	CCG	AGA +	ACC	ACA	GGT	GTA +	CAC	CCT	GCC -+-	CCC	ATC	CCG(	GGA	TGA(	GCTG	420
	301	CGG	GTT	TCC	CGT	CGG	GGC	TCT	TGG	TGT	CCA	CAT	GTG	GGA	CGG	GGG	TAG	GGC	CCT.	ACT	CGAC	
a		A	K	G	Q	P	R	E	P	Q	V	Y	T	L	P	P	S	R	D	E	L	-
	421	AC	CAA	GAA	CCA	GGT	CAG	CCT +	GAC	CTG	CCT	GGT +	CAA	AGG	CTT - + -	CTA	TCC	CAG +	CGA	CAT	CGCC +	480
	101	TG	GTT	СТТ	GGT	CCA	GTC	GGA	.CTG	GAC	GGA	CCA	GTT.	TCC	GAA	.GAT	AGG	GTC	GCT	GTA	GCGG	
a																	P					-
	481				-+-			+				+			-+-			+			GCTG	540
	101	CA	CCT	CAC	CCT	CTC	GTT	'ACC	CGT	'CGG	CCI	CTT	'GTT	'GAT	GTI	'CTG	GTG	CGG	AGG	GCA	CGAC	
a		V	E	W	Е	S	N	G	Q	P	E	N	N	Y	K	Т	Т	P	P	V	L	-
	541				-+-			+	<b>-</b>			+			-+-			+		<del>-</del>	GCAG	600
	241	CT	GAG	GCI	GCC	GAG	GAA	GAA	GGA	GAT	GTC	GTI	CGA	GTG	GCA	CCI	GTT	CTC	GTC	CAC	CGTC	
a		D	S	D	G	S	F	F	L	Y	S	K	L	Т	V	D	K	S	R	W	Q	-

## FIGURE 23B

	601				- + -			+				+			-+-			+			GCAG + CGTC	660
a		Q	G	N	v							Н									Q	-
	661				-+-			+				+			-+-			+			TGAC + ACTG	720
a		K	s	L	s	L	s	P	G	K	G	G	G	G	G	v	E	P	N	С	D	-
																В	amH	I 				
	721				-+-			+				TGA + ACT			- + -			+		77	3	
_		т	ш	7.7	M	T47	107	TA7	•	C	F	┎	P	т.	*							

#### FIGURE 24A

	No	rei   	ቦ ል ጥረ	<u> </u>	ኮር አ	ልሮሮ	CAA	ርጥር፥	ፐርልር	~ ልጥ(	CCA	ኮርጥባ	ኮልጥ(	:ጥር:(	GAZ	እጥG <i>ር</i>	GAZ	ኒጥርብ	ուրդու	GAA	CGT	
	1				- + -			+				+			- +			-+-				60
a			М	v	E	P	N	С	D	I	н	v	M	W	E	W	E	С	F	E	R	-
	61				-+-			+				+			- +			- + -			CTC + GAG	120
a		L	G	G	G	G	G	D	ĸ	Т	н	Т	С	P	P	С	P	A	P	E	L	-
	121				- + -			+			<b></b> -	+			-+			· <b>-</b> + ·			TCC + SAGG	180
a		L	G	G	P	S	V	F	L	F	P	P	K	P	K	D	T	L	M	I	S	-
	181				-+-			+		<b>-</b>		+			-+	- <b>-</b> -		+ -	<b>-</b> -		AAG + TTC	240
a		R	Т	P	E	V	T	С	v	V	v	D	V	S	H	E	D	P	E	V	K	-
	241				-+-			+				+			-+-	<b></b> -		+ -			GAG + CTC	300
a		F	N	W	Y	v	D	G	v	E	V	Н	N	A	K	T	K	P	R	E	E	-
	301				-+-			+				+			- + - ·	:	:	+ -		. <b></b> -	GAC	360
a		Q	Y	N	S	Т	Y	R	V	V	S	V	L	Т	V	L	Н	Q	D	W	L	-
	361			- <b>-</b> -	-+-			+				+			- +			+ -			AAA + TTT	420
a		N	G	K	Ė	Y	K	С	K	V	S	N	ĸ	A	L	P	Α	P	I	Е	K	-
	421				-+-			+				+			-+-		<b></b> - ·	+ -	·		TCC + AGG	480
a		Т	I	S	K	A	K	G	Q	P	R	E	P	Q	v	Y	Т	L	P	P	S	-
	481				-+-			+				+			-+-			+ -			CCC + LGGG	540
a		R	D	E	L	Т	K	N	Q	V	s	L	T	С	L	v	K	G	F	Y	P	-
	541				-+-			+				+			-+-	·		+		. <b></b> -	ACG + STGC	600
a		s	D	I	A	v	E	W	E	s	N	G	Q	P	E	N	N	Y	ĸ	T	T	-

## FIGURE 24B

	601				-+-			+				+			-+-			+			CAAG + GTTC	660
a		P	P	v	L	D	s	D	G	s	F	F	L	Y	s	ĸ	L	Т	v	D	K	-
	661				-+-			+				+			-+-			+			CAAC + GTTG	720
a		s	R	W	Q	Q	G	N	v	F	S	С	S	V	M	Н	E	A	L	Н	N	-
		CA	СТА	CAC	GCA	GAA	GAG	CCT	CTC	CCT	GTC	TCC	:GGG	TAA	АТА	- ACT	amH 'CGA	 .GGA	TCC	<u>.</u>		
	721				-+-			+				+			-+-			+	'AGG	77	3	
_		и	v	TT.	0	v	G	т.	Q	T.	S	P	G	ĸ	*							

#### FIGURE 25A

	Nd	eI I																			
	1	CATAT	GGA	CAA	AAC'	TCA	CAC	ATG	rccz	ACCI	rTG1	rcc <i>i</i>	AGCT	rcco	GA/	CTC	CTC	GGG	GGA	CCG	60
	1	GTATA	CCT	GTT'	TTG.	AGT	GTG	TAC	AGG'	rggz	AAC	AGGT	rcg <i>i</i>	AGGC	CTI	rGAC	GAC	ccc	CCT	'GGC	
a		M	D	K	Т	Н	т	С	P	P	С	P	A	P	E	L	L	G	G	P	-
		TCAGT					CCC.	AAA	ACC	CAAC	GGA	CAC	ССТО	CATO	SATO	CTCC	CCG	SACC	CCT	GAG	120
	61	AGTCA	AGAA	GGA	GAA	.GGG	GGG	TTT	rgg	GTT(	ССТО	3TG(	GGA(	3TAC	CTAC	SAGO	GCC	CTGC	GGA		
a		s v	F	L	F	P	P	K	P	ĸ	D	т	L	M	I	s	R	${f T}$	P	E	-
		GTCAC	CATG	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA	AGA	ccc:	rgac	GT(	CAAC	STTC	CAAC	CTGC	TAC	100
	121	CAGTO	STAC	GCA	CCA	CCA	.CCT	GCA	CTC	GGT	+ GCT	rct(	GGG	ACT(	CCA	STT	CAA	зтто	SACC	CATG	100
a		V T	С	v	v	v	D	v	s	н	E	D	P	E	v	ĸ	F	N	W	Y	-
		GTGG	ACGG	CGT	GGA	GGT	GCA	TAA	TGC	CAA	GAC	AAA	GCC	GCG	GGA(	GGA	GCA	GTA(	CAAC	CAGC	240
	181	CACCI	rgcc	-+- :GCA	CCT	CCA	+ CGT	ATT.	ACG	GTT(	+ CTGʻ	rtt(	CGG	CGC	CCT	CCT	CGT	CAT	GTT(	STCG	240
a		V D	G	v	E	v	н	N	A	K	т	K	P	R	E	E	Q	Y	N	S	-
		ACGTA	ACCG	TGT	GGT	CAG	CGT	CCT	CAC	CGT	ССТ	GCA	CCA	GGA	CTG	GCT	GAA'	TGG	CAA	GGAG	200
	241	TGCA	rggc	ACA	CCA	GTC	GCA	GGA	GTG	GCA	+ GGA	CGT	GGT	-+- CCT	GAC	CGA	CTT	ACC	GTT(		300
a		т у	R	v	v	s	v	L	т	v	L	Н	Q	D	W	L	N	G	K	E	-
		TACA	AGTG	CAA	GGI	CTC	CAA	CAA	AGC	ССТ	CCC	AGC	CCC	CAT	CGA	GAA	AAC	CAT	CTC	CAAA	360
	301	ATGT'		GTT														GTA	GAG		360
a		у к	С	K	v	s	N	K	A	L	P	A	P	I	E	ĸ	${f T}$	I	s	K	-
		GCCA	AAGO	GCA	\GC(	ccc	SAGA	ACC	ACA	GGT	GTA	CAC	CCT	GCC	CCC	ATC	CCG	GGA	TGA	GCTG	420
	361	CGGT'	TTC	- + - CCGI	CGG	GGG	+ CTCI	TGG	TGT	CCA	+ CAT	GTG	GGA	CGG	GGG	TAG	GGC	CCT	ACT	CGAC	420
a		A K	G	Q	P	R	E	P	Q	v	Y	Т	L	P	P	s	R	D	E	L	-
		ACCA	AGA/	ACCA	AGG7	rcac	3CC1	rgac	CTG	сст	GGT	CAA	.AGG	СТТ	СТА	TCC	CAG	CGA	CAT	CGCC	400
	421	TGGT	TCT	- + - rgg1	 rcc <i>i</i>	AGTO	+ CGGZ	ACTG	GAC	GGA	+ CCA	GTT	TCC	-+- GAA	GAT	AGG	GTC	GCT	GTA	GCGG	480
a		т к	N	Q	V	s	L	т	С	L	v	K	G	F	Y	P	s	D	I	A	-
		GTGG	AGT	GGG <i>F</i>	AGAC	GCA <i>I</i>	ATGO	GCA	GCC	GGA	GAA	CAA	СТА	.CAA	GAC	CAC	GCC	TCC	CGT	GCTG	E 4 O
	481	CACC	TCA	+ - CCC1	CTC	CGT	racc	r CCGI	CGG	CCT	+ CTT	GTT	'GAT	GTT	CTG	GTG	CGG	AGG	GCA	CGAC	340
a		V E	W	E	S	N	G	Q	P	E	N	N	Y	K	${f T}$	т	P	P	v	L	-
		GACT	CCG	ACGO	GCT(	CCT.	rct:	rcci	CTA	CAG	CAA	GCI	CAC	CGT	'GGA	CAA	GAG	CAG	GTG	GCAG	600
	541	CTGA		+-		·		+			+			-+-	CCIT	 CTTT	+ יריירי	 СтС	CAC	CGTC	600
		CIGN	GGC	rece	JGAG	GGA	AGA	AGGE	7GM I	GIC	.G.11	CGA	IG.I.G	GCA	CCI	GII	CIC				

# FIGURE 25B

	601	CAG	GGG	SAAC	CGT	CTT	CTC.														GCAG	660
	001	GTO	ccc	стто	GCA	GAA	GAG														CGTC	
a		Q	G	N	v	F	S	С	S	V	M	Н	E	Α	L	Н	N	Н	Y	T	Q	-
	661				-+-			+				+			-+-			+			GGGT + CCCA	720
A		K	s	L	S	L	S	P	G	K	G	G	G	G	G	С	т	Т	Н	W	G	-
	721		CACO  GTGO		-+-	CTA		+				748										

## FIGURE 26A

	Nd	leĮ																													
	1	CAT	TAT	GTG	CAC	CAC	CCA	CTG(	GGG	TTT	CACC	CTC	TGC	CGGT	rgg <i>i</i>	AGGC	CGGT	'GGC	GAC	AAA	GGT +	60									
-	1	GTA	ATA	CAC	GTG	GTG(	GGT	GAC	CCC	AAA(	GTGC	GAC	CACC	3CC2	ACCI	rcco	3CC#	ACCC	СТС	TTT	CCA										
a			M	С	Т	Т	Н	W	G	F	Т	L	С	G	G	G	G	G	D	K	G	-									
	<i>C</i> 1	GGZ	AGG	CGG'	TGG	GGA	CAA	AAC'	rca(	CAC	ATG	rccz	ACC:	rtgo	CCCZ	AGC	ACCI	GAZ	ACTO	CTC	GGG +	GG + 120									
	61	CC	CCTCCGCCACCCCTGTTTTGAGTGTGTACAGGTGGAACGGGTCGTGGACTTGAGGACCCC																												
a		G	G	G	G	D	K	T	Н	T	С	P	P	С	P	A	P	E	L	L	G	-									
	101	GGZ	ACC	GTC.	AGT	TTT	CCT	CTT	ccc	CCC	AAA	ACC	CAA	GGA(	CAC	CCT(	CATO	GAT(	CTC	CCGC	SACC	180									
	121	CC	rgg	CAG	TCA	AAA	GGA	GAA	GGG	GGG'	TTT:	rgg	GTT	CCT	GTG	GGA(	GTA(	CTAC	GAG	3GC(	CTGG	100									
a		G	P	s	v	F	L	F	P	P	K	P	K	D	T	L	M	I	S	R	T	-									
	101	CC	rga	GGT	CAC	ATG	CGT	GGT	GGT	GGA	CGT	GAG	CCA	CGA	AGA	CCC'	TGA	GGT( +	CAA	GTT(	CAAC	240									
	181	GG	ACT	CCA	GTG	TAC	GCA	CCA	CCA	CCT	GCA	CTC	GGT	GCT'	TCT	GGG.	ACT	CCA	GTT(	CAA	GTTG	. – •									
a		P	E	V	Т	С	v	V	V	D	V	S	Н	E	D	P	E	V	K	F	N	-									
	241			.CGT	GGA	.CGG	CGT	GGA	GGT	GCA	TAA'	TGC	CAA	GAC.	AAA - + -	GCC	GCG(	GGA(	GGA	GCA(	GTAC	300									
	241	AC	CAT	GCA	CCT	GCC	GCA	CCT	CCA	CGT	ATT.	ACG	GTT	CTG	TTT	CGG	CGC	CCT	CCT	CGT	CATG										
a		W	Y	V	D	G	v	E	V	Н	N	A	K	T	K	P	R	E	E	Q	Y	-									
	301	AA	AACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGC														360														
		TT	GTC	GTG	CAT	'GGC	ACA	CCA	GTC	GCA	.GGA	GTG	GCA	GGA	.CGT	GGT	CCT	GACCGACTTACCG													
a		N	S	Т	Y	R	v	V	S	V	L	Т	V	L	Н	Q	D	W	L	N	G	-									
	361		GGA	GTA	CAA	GTC	CAA	.GGT	CTC	CAA	CAA	AGC +	CCT	CCC	AGC	ccc	CAT	CGA +	GAA	AAC	CATC	420									
		TТ	CCI	CAT	GTI	CAC	GTI	'CCA	GAG	GTT	GTT	TCG	GGA	.GGG	TCG	GGG	GTA	GCT	CTT	TTG	GTAG	G									
a		K	E	Y	K	С	ĸ	V	s	N	K	A	L	P	A	P	I	Ε	K	Т	I	-									
	421		TCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGAT															480													
	421	AG	GTI	TCC	GTT	TCC	CCGI	CGG	GGC	TCT	'TGG	TGT	CCA	CAT	GTG	GGA	.CGG	GGG	TAG	GGC	CCTA										
a		S	K	A	K	G	Q	P	R	E	P	Q	V	Y	Т	L	P	P	S	R	D	-									
	481	GA	GC1	GAC	CAA	AGA?	ACCA	GGT	CAC	CCI	GAC	CTG +	CCT	'GGT	CAA -+-	AGG	CTT	CTA +	TCC	CAG	CGAC	540									
		CT	'CG <i>I</i>	ACTO	GT1	CTT	rggi	CCA	AGTO	GGA	CTG	GAC	GGA	CCA	GTI	TCC	'GAA	GAT	'AGG	GTC	GCTG	CTG									
a		E	L	T	K	N	Q	V	S	L	T	С	L	V	K	G	F	Y	P	S	D	-									
	541	ΑΊ	CGC	CCG	rgg <i>i</i>	AGT	GGG <i>I</i>	AGAC	CAF	TGC	GCA	.GCC	GGA	GAA	CAA	CTA	CAA	GAC	CAC	GCC	TCCC	600									
		TA	GCC	GGC <i>I</i>	ACCI	CAC	CCCI	CTC	CGTT	CACC	CCGT	CGG	CCI	CTT	rgtī	'GA'I	GTT	CTG	GTG	CGG	AGGG										
a		I	Α	V	Е	W	E	S	N	G	Q	P	E	N	N	Y	K	T	T	P	P	-									



## FIGURE 26B

	601				-+-			+				+			-+-			+			CAGG + GTCC	660
a		v	L	D	s	D	G	S	F	F	L	Y	s	K	L	T	V	D	K	S	R	-
	661				- + -			+				+			- + -		<b></b> -	+			CTAC + GATG	720
a		W	Q	Q	G	N	v	F	s	С	s	v	M	н	E	A	L	Н	N	Н	Y	-
	BamHI																					
	721	ACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAATGGATCC																				
2		т	0	ĸ	g	т.	g	т.	S	P	G	ĸ	*									